



EP 03/5896



INVESTOR IN PEOPLE

**PRIORITY DOCUMENT**  
SUBMITTED OR TRANSMITTED IN  
COMPLIANCE WITH  
RULE 17.1(a) OR (b)

The Patent Office  
Concept House  
Cardiff Road  
Newport  
South Wales  
NP10 8QQ

REC'D 18 AUG 2003

WIPO PCT

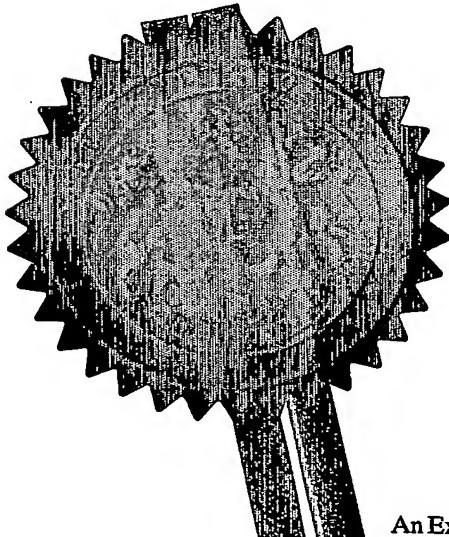
I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

I also certify that the attached copy of the request for grant of a Patent (Form 1/77) bears an amendment, effected by this office, following a request by the applicant and agreed to by the Comptroller-General.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

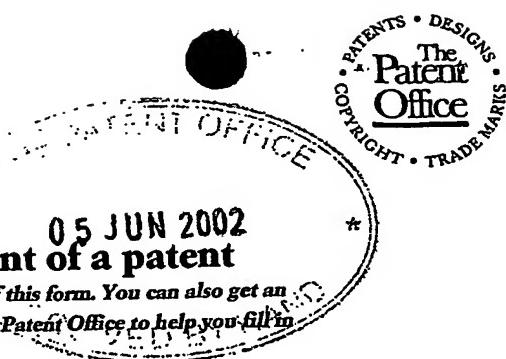
Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.



Signed

Dated 10 June 2003

BEST AVAILABLE COPY

06 JUN 02 272593-1 803006  
P01/7700 010-0218576.705 JUN 2002  
**Request for grant of a patent**

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

**The Patent Office**Cardiff Road  
Newport  
South Wales  
NP10 8QQ

## 1. Your reference

SH-58155

## 2. Patent application number

(The Patent Office will fill in this part)

0212876.7

05 JUN 2002

## 3. Full name, address and postcode of the or of each applicant (underline all surnames)

Walcom Animal Science (I.P.4) Limited  
Unit 714, 7/F, Miramar Tower  
1-23 Kimberly Road  
Tsimshatsui, Kowloon, Hong Kong

H612 Patents ADP number (if you know it)

8400673001

M If the applicant is a corporate body, give the country/state of its incorporation

MAURITIUS

## 4. Title of the invention

Antibodies to Adipose Tissues

## 5. Name of your agent (if you have one)

Lloyd Wise, ~~Deasey & Lloyd~~  
Commonwealth House  
1-19 New Oxford Street  
London WC1A 1LW  
England117001  
Patents ADP number (if you know it)

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and (if you know it) the or each application number

Country

Priority application number  
(if you know it)Date of filing  
(day / month / year)

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application

Date of filing  
(day / month / year)

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? (Answer 'Yes' if:

YES

- a) any applicant named in part 3 is not an inventor, or
- b) there is an inventor who is not named as an applicant, or
- c) any named applicant is a corporate body.

See note (d))

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form.  
Do not count copies of the same document

Continuation sheets of this form

Description 27

Claim(s) 5

Abstract 1

Drawing(s)

10. If you are also filing any of the following, state how many against each item.

Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (*Patents Form 7/77*)

Request for preliminary examination and search (*Patents Form 9/77*)

Request for substantive examination  
(*Patents Form 10/77*)

Any other documents  
(please specify)

11.

I/We request the grant of a patent on the basis of this application.

Signature

Lloyd Wise, Tregear & Co

Date

5 June 2002

12. Name and daytime telephone number of person to contact in the United Kingdom Mr. Geoff Chisholm  
44 207 571 6200

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

- a) If you need help to fill in this form or you have any questions, please contact the Patent Office on 08459 500505.
- b) Write your answers in capital letters using black ink or you may type them.
- c) If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.
- d) If you have answered 'Yes' Patents Form 7/77 will need to be filed.
- e) Once you have filled in the form you must remember to sign and date it.
- f) For details of the fee and ways to pay please contact the Patent Office.

ANTIBODIES TO ADIPOSE TISSUESField of Invention

The present invention relates to antibodies to adipose tissues and in particular polyclonal antibodies to adipocyte plasma membrane proteins in adipose tissues in animals (e.g., farm animals) and/or humans. The present invention also relates to a method of preparing the antibodies and use of such antibodies for the manufacture of a medicament, composition or feed additive for consumption by farm animals and/or humans. The present invention can be applied in providing a method for the treatment of obesity or related conditions.

Background of the Invention

In animal farming, one of the main objectives is to increase the growth rate of the farm animals such that under generally the same conditions of husbandry, the animals will grow faster and as such productivity of the animal farm can be increased. In the past, before modern technology has been adopted in animal farming, farmers would normally simply feed the animals with more food in the hope that higher food consumption would cause the animals to grow and increase in weight faster. However, there is a limit to the extent that such methods can help in increasing the body weight of the animals. Besides,

the drawback is that this method would increase the total consumption of animal feed and accordingly undesirably translate to higher operation costs.

5 Another method to promote growth in farm animals is to administer growth hormones to the animals. This method is however undesirable for a number of reasons. Firstly, growth hormones from different animals are seldom homogenous and different mammalian animals, for example,  
10 only react to certain types of specific growth hormones.  
Since suitable exogenous growth hormones are normally extracted from pituitary glands, it is rather difficult and uneconomical to prepare sufficient quantity of suitable exogenous growth hormones for use on a large-  
15 scale application. Although exogenous growth hormones can now be prepared using DNA recombinant technology, exogenous growth hormones manufactured by such method are still rather expensive. Secondly, the administration of exogenous growth hormones into farm animals is normally performed by direct injection, which is inevitably rather  
20 costly and difficult to administer in a large farm with animals in tens of thousands. Thirdly, it is rather difficult to control the dose administered to produce precisely the desired effect, and an overdose of  
25 exogenous growth hormones is likely to be harmful to the animals. Fourthly, residuals of these exogenous growth

hormones may be passed to the meat products and subsequently to humans through consumption thereof. Further studies in this regard are required although some scientists are concerned about the negative side effects 5 of these exogenous growth hormones to humans.

Various feed additives have also been proposed to be added to animal feed such that animals fed with these feed will grow faster. Unfortunately, regardless which 10 of the above methods is used, it is often the case that a relatively large percentage of the increased body weight results from an increase in fat content and not from lean muscle content. This problem is particularly prominent in swine although other farm animals have similar 15 problems. As humans have become more health conscious nowadays, there is little demand, if any, for meat products having a high fat content. There is therefore a growing demand for meat products having as low a fat content as possible (i.e. high content of lean muscle).

20

Numerous methods have been proposed to cause farm animals to develop with higher muscle content. A very old method is to raise the animals in an open or semi-open farm such that the animals would have more opportunity to exercise 25 such that the fat content in their body may be reduced. However, this method is nearly impossible to carry out in

practice in modern farms wherein space is at a premium. Besides, this method is rather unpredictable. Animals subjected to this method may still have a rather high fat content in their body.

5

Hence, there continues to exist a need for a substance for regulating and reducing the fat content in farm animals. Preferably, the substance should be easy to administer and natural, and should not have any side effects similar to those caused by artificial or exogenous growth hormones. In other words, the substance should be safe to administer. A substance, which works in farm animals, should preferably also work in humans with modifications.

15

It is thus an object of the present invention in which the above issues are addressed, or at least to provide a useful alternative to the public.

20 Summary of Invention

According to a first aspect of the present invention, there is provided antibodies that specifically bind adipose tissues in a target subject which is a farm animal or a patient in need of said antibodies for modulating the content of the adipose tissues in said target subject. Preferably, the antibodies may bind to

characterizing components of plasma membrane of the adipose tissues. The antibodies may bind to granular viscosity proteins and/or fiber viscosity proteins of the adipose tissues.

5  
suitably, the antibodies may be obtained from and/or comprised in eggs of an egg-laying animal. The antibodies may be produced from within the body of the egg-laying animal. The antibodies may be deposited to 10 the eggs of the egg-laying animal. Suitably, the antibodies may be obtained from and/or comprised in eggs of an egg-laying animal. The egg-laying animal may be considered as a production animal. In particular, hens are preferably used due to their relatively high yield of 15 eggs. The advantage is that the eggs laid by the production animal may have become a warehouse of the antibodies of interest.

The antibodies may be produced from within the body of 20 the egg-laying animal. The antibodies may be produced in response to an antigen administered to the egg-laying animal. The antibodies may be prepared from adipose tissues of a source animal. The antigen may comprise plasma membrane and/or its adipocyte plasma membrane 25 surface proteins of the adipose tissues of the source animal.

Preferably, the target subject and said source animal may belong to a same species. Alternatively, the target subject and the source animal may belong to closely related species.

However, the source animal and the egg-laying animal may preferably belong to distinctly different species.

10 Advantageously, the antibodies may be polyclonal antibodies.

According to a second aspect of the present invention, there is provided a feed additive comprising an effective amount of antibodies described above. The feed additive may be adapted to lower the content of the adipose tissues in the target subject.

According to a third aspect of the present invention, 20 there is provided a medicament comprising a pharmaceutically effective amount of antibodies described above. The medicament may preferably be adapted to be administered via ingestion. Alternatively, the medicament may be adapted to be administered via 25 injection.

According to a fourth aspect of the present invention, there is provided a method of modulating content of adipose tissues in the body of a target subject which is a farm animal or a patient in need of antibodies comprising a step of administering a pharmaceutically effective amount of the antibodies that specifically bind the adipose tissues in the target subject. The modulation of the content of the adipose tissues may include at least reducing the content of the adipose tissues in terms of weight percentage in the target subject. This is achieved by interfering the physiological development of the adipose tissues.

The method may comprise a step of binding the antibodies to characterizing components of plasma membrane of the adipose tissues. In particular, the method may comprise a step of binding the antibodies to granular viscosity proteins and/or fiber viscosity proteins of said adipose tissues.

20

Preferably, the method may comprise a step of administering the composition via ingestion. Alternatively, the method may comprise a step of administering the composition via injection.

25

Advantageously, the antibodies may be polyclonal antibodies.

According to a fifth aspect of the present invention,  
5 there is provided a method of manufacture a composition comprising a pharmaceutically effective amount of antibodies described above comprising a step of obtaining the antibodies from eggs of an egg-laying animal. The method may comprise a step of allowing deposition of the  
10 antibodies to the eggs of the egg-laying animal.

Preferably, the method may comprise a step of causing production of the antibodies from within the body of the egg-laying animal. The method may comprise a step of causing production of the antibodies in the egg-laying animal in response to an antigen prepared from adipose tissues of a source animal. This is due to immunological responses to the antigen by the body of the egg-laying animal.

20

The method may comprise a step of administering the antigen to the egg-laying animal. Suitably, the antigen may comprise plasma membrane and/or its adipocyte plasma membrane surface proteins of the adipose tissues of the  
25 source animal.

Preferably, the target subject and the source animal belong to a same species. Alternatively, the target subject and the source animal belong to closely related species. The source animal and the egg-laying animal 5 belong to distinctly different species. The produced antibodies may preferably be polyclonal antibodies.

Preferably, the composition may comprise egg yolk containing the antibodies.

10

Preferably, the antigen may be prepared from adipose tissues of a source animal. The antigen may comprise plasma membrane and/or its adipocyte plasma membrane 15 surface proteins of the adipose tissues of the source animal.

Advantageously, the target subject and the source animal may belong to a same species. Alternatively, the target 20 subject and the source animal may belong to closely related species. While the target subject and the source animal may be different species, the more closely related they are, the more effective the antibodies are in achieving their effects.

Advantageously, the source animal and the egg-laying animal may belong to distinctly different species. The less closely related they are, the more effective the antibodies are in achieving their effects.

5

The antibodies may preferably be polyclonal antibodies.

Detailed Description of the Invention

As discussed above, a biological substance (e.g. growth 10 hormone) may be produced and extracted from the pituitary glands of a "production" animal. Depending on the type or nature of the biological substance, they may actually be obtained or isolated using different methods. For instance, if the biological substance is a growth hormone 15 which is present in the colostrum of cow milk in a production animal, an appropriate isolation procedure of the growth hormone therefrom is to be performed. Alternatively, if the growth hormone is present in the blood serum in a production animal, an alternate suitable 20 isolation procedure of the growth hormone therefrom is to be performed. However, whichever isolation procedure is used, it has been found that isolation of a sufficient quantity of biological substance of interest for commercial use from an animal source is very difficult. 25 The difficulty arises firstly because the quantity of biological substance produced is usually very small.

Secondly, isolation of biological substance from the animal is very costly. The same difficulty similarly exists in the extraction or isolation of specific antibodies of interest from an animal.

5

The present invention is based on the demonstration that antibodies when administered to a target subject which may be a farm animal reduce or at least modulate the overall fat content in its body to a more desired level 10 and thus to produce leaner meat. When the present invention is applied for use in humans, the target subject means a patient in need of the antibodies.

Generally, adipose tissues are firstly removed from a 15 source animal. Plasma membrane of the adipose tissues is then isolated from the adipose tissues. The isolated plasma membrane includes all its adipocyte plasma membrane proteins and recognition sites such as granular and fiber viscosity proteins. The isolated plasma 20 membrane is used to prepare a substance for use as an antigen. The substance is preferably in a form suitable for injection and is engineered to have an immunologically effective concentration of the antigen which is adapted to elicit a desired immunological 25 response in a production animal.

The substance is then administered to the production animal which is an egg-laying animal such as a hen. The use of hen as production animal is particularly preferable because a hen normally produces more eggs than other egg-laying fowls. For instance, an average hen in a commercial farm can often lay as many as 200 to 300 eggs per year. However, other egg-laying animals such as ducks may also be used. The amount of egg yolk produced by a hen is accordingly very significant.

10

Once the substance containing the antigen is administrated to the production animal such as by injection, the body of the production animal will react and initiate an immune response to the antigen by producing antibodies. As described above, the antigen of the administered substance actually comprises the plasma membrane of the adipose tissues from the source animal. The antibodies produced by the egg-laying animal are thus polyclonal and adapted to bind various different characterizing components, i.e. the adipocyte plasma membrane proteins of the plasma membrane. During the research and development of the present invention, it has been identified that a relatively significant amount of the antibodies produced are deposited in the eggs which are subsequently laid by the production animal. It has further been identified that the egg yolk of the eggs has

a much higher concentration of the antibodies than the egg white indicating that there is a preferential deposition of the antibodies in the egg yolk. In other words, the problem of producing and isolating a biologically useful substance from an animal source is addressed in the context of the present invention. In particular, the eggs can be seen as a warehouse in which the antibodies of interest can be retrieved.

The produced antibodies can be isolated from the egg yolk. Alternatively, the raw egg yolk containing the antibodies may be used directly or after processing such as by subjecting it to desiccation to form egg yolk powder. An effective amount of the isolated antibodies, the raw or processed egg yolk containing the antibodies is then administrated to a target subject. One main application of the present invention is intended to be in animal farming and in this case the target subject may be a farm animal. However, as indicated above, the present invention may also be applied for use in humans and thus the target subject may be a patient in need of the antibodies in such context. When administered to the target subject, the antibodies will bind to characterizing structures or domains (e.g. the surface proteins of cells in the target animal) which are similar to the adipocyte plasma membrane proteins of the adipose

tissues of the source animal. For instance, if the source animal is a swine and the target subject belong to the same species of swine, the administered antibodies will bind to the adipocyte plasma membrane proteins of the adipose tissues in the body of the target subject and interfere with the physiological development of its adipose tissues. It has been identified during the research and development of the present invention that such binding and/or interference significantly decrease the content of adipose tissues in the target subject both in terms of weight percentage and absolute weight.

As indicated above, the source animal and the target subject may belong to the same species of animals. The more closely related of the source animal and the target subject are, the more effective the produced antibodies are for targeting adipose tissues of the target subject and in eventually reducing or at least modulating the fat content in the body of the target animal. However, the source animal and target subject need not belong to the same species. For example, the source animal may be a cow but the target animal may be a swine. Since both cows and swine are mammals, their adipose tissues and in particular the plasma membrane thereof have more resemblance than between for example the adipose tissues of an avian and a mammal. In summary, the more closely

related the source animal and target subject are, the more effective the produced antibodies are in binding, interfering, modulating and/or reducing the fat content in the body of the target subject.

5

It is however to be noted that the source and production animals should preferably be sufficiently different. Otherwise, the substance containing the antigen administered to the production animal would not elicit an effective immunological response to produce a sufficient amount of antibodies of interest. For instance, if the source animal is a duck, the antigen prepared from its adipose tissues will elicit a relatively low immunological response in a hen.

15

The present invention is described in further detail by way of the following experiments.

#### EXPERIMENTS

20

##### Experiment I: Procedures for Producing Antibodies to Adipose Tissues of Swine in Hens

A. Isolation of plasma membrane from adipose tissues of a source animal

25 Adipose tissues were removed from the back of a source animal. The source animal used in the experiment was an

Erhualian pig. The adipose tissues were treated and homogenized in an extraction medium at around 37°C in a Waring blender at 2000 rpm for 5 min and then treated with ultrasound for 10 minutes. The extraction medium 5 was made of 0.25M of sucrose, 0.01M of Na<sub>2</sub>HPO<sub>4</sub>, 0.002M EDTA, 0.2mM PMSF and adjusted to pH7.4 at 40°C. The homogenate was then centrifuged at 5000 rpm for 30 minutes at 37°C to separate the triglyceride from the other components.

10

The supernatant containing the triglyceride was then removed after centrifugation and the remainder, i.e. the infranatant, was subjected to centrifugation at 10000 rpm for 30 min at 4°C. The supernatant thereof was then 15 subjected to centrifugation at 10000 rpm for 30 minutes at 4°C and the supernatant was retained. The supernatant was then subjected to centrifugation at 38000 rpm for 1 hour at 4°C. The plasma membrane including its adipocyte membrane proteins from the adipose tissues was obtained. 20 The membrane proteins were then stored at -20°C until they were used.

B. Production of antibodies to pig adipocyte plasma membrane and its proteins

25 The plasma membrane obtained from the above procedure was used to prepare an antigen to elicit immune response from

production animals. In this experiment, egg-laying hens were used. In the experiment, an initial injection comprising the antigen was prepared to contain approximately 80 $\mu$ g of the plasma membrane and its proteins initially suspended in 0.5ml of complete Freund's adjuvant. A second injection comprising the same antigen suspended in incomplete Freund's adjuvant for boosting the immune response was subsequently administered also by direct injection. Each round of administration was performed in at least 20 different intercutaneomucous sites of the production animals at intervals of once every four weeks. After the third and fourth booster injections, egg yolk was subsequently obtained from eggs laid by the hens. Antibody responses of the egg yolk were then assessed.

C. Enzyme immunoassay of egg yolk antibodies to plasma membrane of pig adipocytes

The egg yolk antibodies were prepared and screened for antibody titer against a suitable adipocyte plasma membrane, and for cross reactivity with liver, kidney, red blood cells and skeletal muscle by ELISA. 100 $\mu$ l of the plasma membrane containing 0.25 $\mu$ g of the adipocyte plasma membrane proteins in carbonate-buffered solution was coated onto each well of 96-well polystyrene plates. The plates were kept overnight at 4°C in a humidified

chamber. The wells were then emptied and blocked with PBS containing 0.05% Tween 20 for three times. 100 $\mu$ l of the egg yolk diluted in PBST was added to each well. The plates were kept for 1 hour at 37°C and subjected to 5 washing with PBST for three times. 100 $\mu$ l of rabbit anti-chicken IgG HRP conjugate diluted to 1:5000 in PBST was added to each well. The plates were incubated for 1 hour at 37°C. The plates were washed three times with PBST. 100 $\mu$ l of O-phenylenediamin (OPD) substrate (1.5mg/ml) was then added to each well. The plates then were incubated at 37°C for 5 to 10 minutes, and the reaction in each well was stopped with 50ul of 2M H<sub>2</sub>SO<sub>4</sub>. Absorbance was measured at 490nm using an ELA plate reader. Each assay was performed in duplicate and repeated three times. It 15 was found that the titer of the antibodies in the egg yolk was more than 1:12800 which is considered as a relatively high titer value in the context of the present invention.

20 Experiment II: Effect of adipose tissues antibodies on body weight of target animal

A. Background

The target animal used in this experiment was laboratory rats. Ninety-six female rats were used in the experiment 25 with an average body weight of 140g. The rats were divided equally and randomly into four groups. The rats

were kept in sub-groups of three in cages. The rats were fed with regular rat feed. The experiment commenced on 30 September 2001 and ended on 14 December 2001.

5    B. Procedure

The four groups of rats consist of two test groups and two respective control groups. The two test groups include a first test group in which each rat was subjected to injection of raw egg yolk containing the 10 adipose tissue antibodies subcutaneously in different locations at their back. The egg yolk adipose tissue antibodies were obtained based on similar procedures described in the above Experiment I. The dose of each injection was 1ml per rat per day. Each round of 15 administration includes one injection each day for four consecutive days. The egg yolk was administered again once a month during the experiment. The titer of the antibodies in the raw egg yolk was more than 1:12800.

20    The second test group was administered with the same dose, concentration and frequency of the egg yolk adipose tissue antibodies but by oral ingestion instead of injection.

There is a corresponding control group for each of the two test groups of rats. The control groups of rats were administered with regular raw egg yolk.

5

### C. Results

The following tables show the results of the experiment.

TABLE 1: Effects of the egg yolk adipose tissue  
10 antibodies on body weight and feed conversion rate ( $X \pm SE$ )

	Beginning body weight (g)	Ending body weight (g)	Body weight gain (g)	Food intake (g)	Feed conversion rate
First test group (by injection)	163.42 $\pm$ 2.55	297.64 $\pm$ 5.23	133.91 $\pm$ 4.23	22.25 $\pm$ 0.23	6.25 $\pm$ 0.20
First control group (by injection)	162.88 $\pm$ 2.28	289.00 $\pm$ 5.33	126.62 $\pm$ 4.40	21.87 $\pm$ 0.26	6.27 $\pm$ 0.30
Second test group (by ingestion)	159.10 $\pm$ 2.70	281.56 $\pm$ 7.43	122.25 $\pm$ 5.02	21.75 $\pm$ 0.23	5.87 $\pm$ 0.22
Second control group (by ingestion)	164.21 $\pm$ 2.00	292.82 $\pm$ 6.54	127.18 $\pm$ 6.20	21.72 $\pm$ 0.52	6.52 $\pm$ 0.21

TABLE 2: Effects of the egg yolk adipose tissue antibodies on fat content in various parts of the rat body ( $X \pm SE$ )

	Omental and mesenteric fat Content (%)	Parametrial fat Content (%)	Perirenal fat Content (%)	Gastrocnemius fat Content (%)
First test group (by injection)	$18.06 \pm 0.72^{\text{aa}}$	$26.43 \pm 1.72^{\text{aa}}$	$17.95 \pm 1.48^{\text{aa}}$	$6.03 \pm 0.11^{\text{a}}$
First control group (by injection)	$18.75 \pm 0.87^{\text{aa}}$	$27.58 \pm 1.78^{\text{aa}}$	$19.18 \pm 1.32^{\text{aa}}$	$5.73 \pm 0.06^{\text{b}}$
Second test group (by ingestion)	$14.22 \pm 1.02^{\text{bb}}$	$18.63 \pm 1.98^{\text{bb}}$	$12.01 \pm 1.17^{\text{bb}}$	$5.89 \pm 0.11$
Second control group (by ingestion)	$17.16 \pm 1.05^{\text{a}}$	$24.58 \pm 2.24^{\text{a}}$	$15.32 \pm 1.25^{\text{a}}$	$5.83 \pm 0.09$

5 KEY:

Values bearing different superscripts are significantly different; A,  
B means  $P < 0.01$ ; a, b means  $P < 0.05$

TABLE 3: Effects of the egg yolk adipose tissue antibodies on level of triglyceride, cholesterol and fatty acids in blood of the rat body ( $X \pm SE$ )

	Triglyceride (mg/dl)	Total cholesterol (mg/dl)	Total fatty acids ( $\mu\text{mol/L}$ )
First test group (by injection)	$33.83 \pm 1.70^{\text{aa}}$	$61.05 \pm 3.56$	$140.69 \pm 9.73$
First control group (by injection)	$45.42 \pm 2.67^{\text{b}}$	$58.91 \pm 2.44$	$135.29 \pm 7.31$
Second test group (by ingestion)	$32.00 \pm 1.60^{\text{aa}}$	$61.35 \pm 2.61$	$161.21 \pm 8.05^{\text{a}}$
Second control group (by ingestion)	$41.20 \pm 2.48^{\text{b}}$	$54.64 \pm 4.21$	$121.72 \pm 7.47^{\text{b}}$

KEY:

5 Values bearing different superscripts are significantly different; A,  
B means  $P < 0.01$ ; a, b means  $P < 0.05$

#### D. Conclusion and discussion

In Table 1, it is shown that the administration of the  
10 antibodies by injection increased the weight gain and the  
food consumption in the first test group of rats when  
compared to the corresponding control group by 5.8% and  
by 1.7% respectively. The feed conversion rate was  
however decreased by 0.32%. It is also shown that the

administration of the antibodies by ingestion when compared to the corresponding control group decreased the weight gain in the second test group of rats by 3.9% and increased the food consumption by 0.14%. The feed conversion rate was decreased by about 10%. The experimental data in relation to the first test and control groups illustrates that the administration of the antibodies by injection increased the body weight slightly although the feed conversion rate was lowered very slightly. A low feed conversion rate means that less amount of feed is required to produce a unit of body weight. The experimental data in relation to the second and test and control groups illustrates that the administration of the antibodies by ingestion decreased the body weight gain slightly and the feed conversion efficiency was substantially decreased by 10%. This is important and demonstrates that the administration of the antibodies through ingestion is more effective in reducing the overall body weight slightly but lowering the feed conversion rate very significantly.

Referring to Table 2, it is shown that the administration of the antibodies by injection caused to the fat content of their omental and mesenteric, paramentrial and perirenal tissues to decrease by 3.7%, 4.2% and 6.4% respectively when compared to the corresponding control

groups. However, the fat content of the gastrocnemius was increased by 5.2%. It is also shown that the administration of the antibodies by ingestion very significantly decreased the fat content of their omental and mesenteric, parametrial and perirenal tissues by 5 17.1%, 24.2% and 2.16% respectively when compared to the corresponding control group.

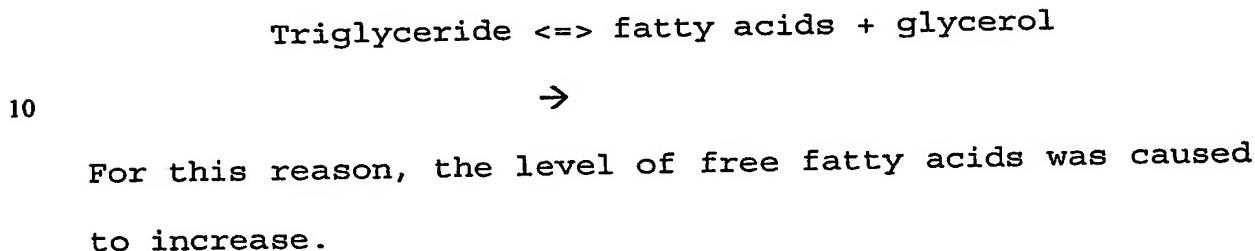
As clearly shown, the administration of the antibodies by 10 whichever means, injection or ingestion, is generally effective in reducing the fat content in various parts of the body in the animal. In particular, it is shown that administration by way of ingestion is significantly more effective in reducing the general fat content of the 15 animal.

Referring to Table 3, it is shown that the administration of the antibodies by injection caused the level of triglyceride to decrease significantly by 25.5%. The 20 levels of cholesterol and free fatty acids were caused to rise marginally by 3.6% and 4.0% respectively. In relation to the administration of the antibodies through oral ingestion, the level of triglyceride was caused to decrease also significantly by 22.3%. The levels of 25 cholesterol and free fatty acids were caused to increase by 12.3% or 32.4 respectively.

When the data of all three tables are considered together, it is clearly shown that the administration of the antibodies into the animal does reduce the overall fat content in its body and this is supported by the decrease in the overall fat content in the test groups of rats shown in Table 2 and the levels of triglyceride shown in Table 3. In particular, it is shown that administration of the antibodies by means of oral ingestion is more effective when compared to that by direct injection.

The above results are significant in two ways. Firstly, surprisingly, the antibodies produced according to the present invention are more effective when administered orally. This is important because the antibodies can in principle be mixed with a standard feed material in animal farming and as such administration thereof will become very easy, effective and yet can achieve its intended function in reducing fat content. Secondly, there are no observable side effects to the animal. For instance, the overall body weight is not affected in any significant way and yet the fat content is reduced. The feed conversion rate is also slightly improved. In other words, there is less fat content and higher lean meat content in the body of the target subject.

In table 3, it is shown that the level of free fatty acids was increased significantly. This can be explained as follows. Triglyceride is composed of fatty acids and 5 glycerol. When the level of triglyceride (i.e. fat content) is caused to be reduced, the equilibrium is shifted to the right as illustrated below.



Based on the findings of the above experiment, the 15 antibodies when administered in animal farming (e.g. via an animal feed) can produce animals with leaner meat. Among most farm animals for producing meat for human consumption, swine tend to have a rather high fat content. Thus, the present invention is particularly 20 suitable to be applied in raising swine.

When applied for use in humans, the antibodies can be used in the manufacture of a medicament or composition for the treatment or prevention of obesity and/or related 25 conditions. Alternatively, the antibodies can be added to a food supplement suitable for consumption by humans.

A medicament comprising such antibodies may also be produced.

The contents of each of the references mentioned above,  
5 are herein incorporated by reference in their entirety.  
It is to be noted that numerous variations,  
modifications, and further embodiments are possible and  
accordingly, all such variations, modifications and  
embodiments are to be regarded as being within the scope  
10 of the present invention and to be understood by the  
persons skilled in the art.

## Claims:-

1. Antibodies that specifically bind adipose tissues in a target subject which is a farm animal or a patient in need of said antibodies for modulating the content of said adipose tissues in said target subject.
- 5 2. Antibodies according to Claim 1 binding to characterizing components of plasma membrane of said adipose tissues.
- 10 3. Antibodies according to Claim 1 or 2 binding to granular viscosity proteins of said adipose tissues.
4. Antibodies according to Claim 1, 2 or 3 binding to fiber viscosity proteins of said adipose tissues.
5. Antibodies according to any preceding claim obtained from and/or comprised in eggs of an egg-laying animal.
- 15 6. Antibodies according to Claim 5 deposited to said eggs of said egg-laying animal.
7. Antibodies according to Claim 5 or 6 produced from within the body of said egg-laying animal.
- 20 8. Antibodies according to Claim 5, 6 or 7 produced in response to an antigen administered to said egg-laying animal.
9. Antibodies according to Claim 8 wherein said antigen is prepared from adipose tissues of a source animal.
- 25 10. Antibodies according to Claim 9 wherein said antigen comprises plasma membrane and/or its adipocyte plasma

membrane surface proteins of said adipose tissues of  
said source animal.

11. Antibodies according to Claim 9 or 10 wherein said  
target subject and said source animal belong to a same  
5 species.

12. Antibodies according to Claim 9 or 10 wherein said  
target subject and said source animal belong to closely  
related species.

13. Antibodies according to any one of Claims 9 to 12  
10 wherein said source animal and said egg-laying animal  
belong to distinctly different species.

14. Antibodies according to any preceding claim wherein  
said antibodies are polyclonal antibodies.

15. A feed additive comprising an effective amount of  
antibodies defined in any one of Claims 1 to 14.

16. A feed additive according to Claim 15 adapted to  
lower the content of said adipose tissues in said  
target subject.

17. A medicament comprising a pharmaceutically effective  
20 amount of antibodies defined in any one of Claims 1 to  
14.

18. A medicament according to Claim 17 adapted to be  
administered via ingestion.

19. A medicament according to Claim 17 adapted to be  
25 administered via injection.

20. A method of modulating content of adipose tissues in the body of a target subject which is a farm animal or a patient in need of antibodies comprising a step of administering a pharmaceutically effective amount of said antibodies that specifically bind said adipose tissues in said target subject.
- 5
21. A method according to Claim 20 comprising a step of binding said antibodies to characterizing components of plasma membrane of said adipose tissues.
- 10 22. A method according to Claim 20 or 21 comprising a step of binding said antibodies to granular viscosity proteins of said adipose tissues.
23. A method according to Claim 20, 21 or 22 comprising a step of binding said antibodies to fiber viscosity proteins of said adipose tissues.
- 15
24. A method according to any one of Claims 20 to 23 comprising a step of administering of said composition via ingestion.
25. A method according to any one of Claims 20 to 24 wherein said antibodies are polyclonal antibodies.
- 20
26. A method of manufacture a composition comprising a pharmaceutically effective amount of antibodies as defined in any one of Claims 1 to 14 comprising a step of obtaining said antibodies from eggs of an egg-laying animal.
- 25

27. A method according to Claim 26 comprising a step of allowing deposition of said antibodies to said eggs of said egg-laying animal.
28. A method according to Claim 26 or 27 comprising a 5 step of causing production of said antibodies from within the body of said egg-laying animal.
29. A method according to Claim 26, 27 or 28 comprising a step of causing production of said antibodies in said egg-laying animal in response to an antigen prepared 10 from adipose tissues of a source animal.
30. A method according to Claim 29 comprising a step of administering said antigen to said egg-laying animal.
31. A method according to Claim 29 or 30 wherein said 15 antigen comprises plasma membrane and/or its adipocyte plasma membrane surface proteins of said adipose tissues of said source animal.
32. A method according to Claim 29, 30 or 31 wherein said target subject and said source animal belong to a same species.
33. A method according to Claim 29, 30 or 31 wherein 20 said target subject and said source animal belong to closely related species.
34. A method according to any one of Claims 29 to 33 wherein said source animal and said egg-laying animal 25 belong to distinctly different species.

35. A method according to any one of Claims 26 to 34  
wherein said antibodies are polyclonal antibodies.
36. A method according to any one of Claims 26 to 35  
wherein said composition comprises egg yolk containing  
5       said antibodies.
37. Antibodies substantially as hereinbefore described  
and as illustrated.
38. A feed additive substantially as hereinbefore  
described and as illustrated.
- 10 39. A medicament substantially as hereinbefore described  
and as illustrated.
40. A method of preparing antibodies for modulating the  
content of adipose tissues in an animal or patient in  
need thereof substantially as hereinbefore described  
15       and as illustrated.

Abstract

Antibodies to Adipose Tissues

Antibodies that specifically bind adipose tissues in a  
5 target subject which is a farm animal or a patient in  
need of said antibodies for modulating the content of  
said adipose tissues in said target subject.

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
- IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- FADED TEXT OR DRAWING**
- BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- SKEWED/SLANTED IMAGES**
- COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- GRAY SCALE DOCUMENTS**
- LINES OR MARKS ON ORIGINAL DOCUMENT**
- REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**